

CLAIMS what is claimed is:

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5/16/02
- 5 ~~BI A~~ 1. A hybrid polyketide synthase ("PKS") gene comprising a first nucleic acid portion or portions encoding at least one domain of a first type I PKS and a second nucleic acid portion or portions encoding at least one type I PKS domain which is heterologous to said first PKS.
- 10 2. A hybrid PKS gene according to claim 1 wherein said first nucleic acid portion encodes at least a loading module and said second nucleic acid portion encodes at least one extension module.
- 15 3. A hybrid PKS gene according to claim 2 wherein said loading module comprises an acyltransferase and an acyl carrier protein.
- 20 4. A hybrid PKS gene according to claim 2 or claim 3 wherein a said first nucleic acid portion encodes a loading module together with the ketosynthase ("KS") domain (only) of the homologous extender module.
- 25 5. A hybrid PKS gene according to claims 2, 3 or 4 wherein said loading module is capable of loading a substrate to produce a starter unit different from a starter unit normally associated with said extension module(s).
- 30 6. A hybrid PKS gene according to any of claims 2-5 wherein said loading module is capable of loading any of a multiplicity of different starter units.
- 35 7. A hybrid PKS gene according to claim 6 wherein said loading module is an avr loading module.
8. A hybrid PKS gene according to any preceding claim

wherein said nucleic acid portions encode combinatorial modules each extending between corresponding domains of two natural modules.

5 9. A hybrid PKS gene according to any preceding claim including nucleic acid encoding a chain terminating enzyme other than thioesterase.

10 10. A hybrid PKS gene according to any preceding claim wherein said second nucleic acid portion or portions comprises a portion encoding an extension module leading to a ketide unit differing from the natural unit in oxidation state and/or stereochemistry and/or substitution pattern.

15 11. Nucleic acid encoding a gene according to any of claims 1-10 operably linked to a PKS type II promoter.

20 12. Nucleic acid according to claim 11 wherein the promoter is accompanied by its natural activator gene.

13. Nucleic acid according to claim 11 or 12 wherein the promoter is act I of S.coelicolor.

25 14. A hybrid polyketide synthase as encoded by a gene according to any of claims 1-10.

30 15. A vector including a gene or nucleic acid according to any of claims 1-13.

16. A transformed organism containing a gene or nucleic acid according to any of claims 1-13 and able to express a polyketide synthase encoded thereby.

35 17. A method of producing an organism as defined in claim 16 comprising the step of introducing a plasmid containing 'donor' DNA into a host cell under conditions

such that there is homologous recombination with heterologous chromosomal PKS DNA.

18. A method of making a polyketide by culturing the organism of claim 16.

19. A polyketide as prepared by the method of claim 18.

20. Use of a type III PKS promoter to control a heterologous gene.

21. Nucleic acid comprising a type II PKS promoter operably linked to a heterologous gene.

22. The use or nucleic acid according to claim 20 or claim 21 wherein the promoter is accompanied by its natural activator gene.

23. The use or nucleic acid according to claim 20, 21 or 22 wherein the promoter is act I of S.coelicolor.